IN THE SPECIFICATION

Applicants present a replacement paragraph below indicating the changes with insertions indicated by underlining and deletions indicated by strikeouts and/or double bracketing.

Please add the following new paragraph after the paragraph beginning on page 7, line 25 as follows. This amendment was made because the formal drawings separate Fig. 9 into Fig. 9 and 9A.

FIG. 9A is a schematic representation of the fringe pattern within the spot of Fig. 9 as seen along line 9A-9A of Fig. 9.

Please replace the paragraph beginning on page 14, line 3 with the amended paragraph as follows. Support for this amendment may be found at least within FIG. 1.

Due to its flexibility, the conformation of a polymer may be constantly changing. As a consequence, each point on the polymer may have a different velocity from another point on the polymer. For polymers in a fluid flow, the velocity of an elongated polymer is also affected by the fluid flow 104. The velocity of a single elongated polymer can be described in various manners.

Please replace the paragraph beginning on page 16, line 21 with the amended paragraph as follows. Reference character 330 was replaced with 329 to delete a duplicate reference character. Fig. 7 was also amended to reflect this change.

In other embodiments, multiple detection zones can be defined by splitting the output of a single laser to create angularly displaced beams. In one embodiment depicted schematically in FIG. 7, a first partially reflecting beamsplitter 320 and a fully reflective mirror 322 can be employed to create two beams 324, 326 that converge on a second partially reflecting beamsplitter 328 which reflects the beams onto the output aperture of a microscope objective

329 [[330]]. The angular separation is controlled by setting the spacing and angles between the first partially reflecting beamsplitter 320 and the fully reflecting mirror 322. In a preferred embodiment, the partially reflecting beamsplitter is a pellicle type of beamsplitter. The very thin membrane of the pellicle means that a ghost beam from the rear surface of the beamsplitter is effectively avoided.

Please replace the paragraph beginning on page 16, line 31 with the amended paragraph as follows. Support for this amendment may be found at least within FIG. 8.

In still another embodiment, such as that shown schematically in FIG. 8, a diffractive optical element such as a phase grating is used to split a monochromatic laser beam into multiple beams at various grating orders, e.g., a zero order (straight through) beam, first order beams and higher order beams. The distribution of energy into the different orders is determined by the depth of grooves formed in the phase grating, whereas the angular separation of different orders of beams is determined by groove spacing. In this embodiment a collimated laser bean is bent by a fully reflective mirror 330 and passed through a phase grating 332. A second optical element, such as a lens 334, is used to collect the diverging beams from a diffractive optics and refocus the beams 336, 338, so that they converge and encounter a partially reflecting beamsplitter 340 and are reflected toward a microscope objective 342 [[340]].

Please replace the paragraph beginning on page 17, line 9 with the amended paragraph as follows. This amendment is being made because the formal drawings separate Fig. 9 into Fig. 9 and 9A.

In yet another embodiment, shown schematically in FIG. 9 and 9A, a fringe pattern of alternating dark and bright bands formed within a single illumination spot 350 is used to define detection zones. An elongated polymer, such as a DNA molecule, moves through the spatially periodic bands. In one preferred embodiment, an elongated polymer is labeled with one or

more fluorescent labels. As the elongated polymer moves through the bands, any bound fluorescent labels will emit fluorescence in proportion to the illuminating light. The movement of the fluorescent labels will therefore result in a temporally periodic emission. The time pattern of emission can be measured, and by knowing the spatial periodicity, i.e., the fringe spacing, the velocity of the DNA can be calculated from the measured temporal periodicity. In a related embodiment, the backbone of an elongated DNA molecule is stained with a fluorescence dye. In this embodiment, a stairstep pattern of emission will be observed as successively more of the bright bands illuminate DNA. While not intending to be limited as such, the fringe pattern can be created by overlapping, in a single illumination spot, two beams 352, 354 that have been formed from a single laser and passing those beams through a microscope objective lens 356, as represented schematically in FIG. 9. The resulting fringe spacing is one half the wavelength of the illuminating light when the two beams are oriented 180 degrees to each other. At other angles, the fringe spacing is larger and can be found from $D = / 2\sin(q)$, where D is the fringe spacing, is the wavelength of the illuminating laser and q is the half-angle between the two laser beams. The illumination spot preferably is a few microns in size such that a sufficient number of fringes are formed.

Please replace the paragraph beginning on page 17, line 29 with the amended paragraph as follows. Support for this amendment may be found at least within FIGS. 3 and 5.

The optical methods described above can also be combined. For example, elongated DNA molecules labeled with both intercalating dye and sequence specific fluorescence markers are contemplated. Preferably, the intercalating dye and the fluorescence markers emit light of different and distinguishable wavelengths. In such an embodiment, signal amplitude profiles 201, 202, 211, 212 illustrated by both FIG. 3 and FIG. 5 are simultaneously determined for a DNA molecule. Any dual color configurations for measuring fluorescence from both the intercalating dye and the fluorescence markers can be used. Such configurations are described, for example, in Deniz et al., 1999, Proc. Natl. Acad. Sci. USA. 96:3670-3675; and Ha et al., 1996, Proc. Natl. Acad. Sci. USA. 93:6264-6268.

Please replace the paragraph beginning on page 24, line 10 with the amended paragraph as follows. Support for this amendment may be found at least within FIG. 4.

However, since the velocity of the polymer may be changing upon passage through the region of interest, it is preferable to provide multiple detection zones along the path of the elongated polymer so that multiple signal amplitude profiles can be obtained. In one embodiment, the spacings between each adjacent pair of detection zones are much smaller than the length of the elongated polymer. In such an embodiment, overlapping signal amplitude profiles along the strand of the elongated polymer can be obtained, permitting determination of time dependent velocity v(t). This will increase the accuracy of the velocity measurements and allow a more accurate measurement of the polymer length. A schematic of the output is shown in the following FIG. 4. In FIG. 4, four signal amplitude profiles 207-210 of an elongated polymer are shown (with arbitrary relative intensities). Any of the different types of velocities can be used in the multiple detection scheme. For instance, velocity determination can further be estimated by using a combination of leading edge velocity information, center-of-mass estimations, rise time estimations, and other information that can be obtained from the intercalator signal.